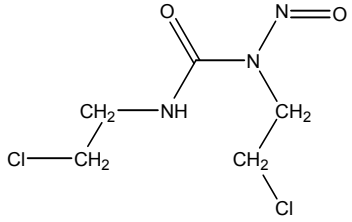
BIS(CHLOROETHYL) NITROSOUREA
CAS No. 154-93-8
First Listed in the *Fourth Annual Report on Carcinogens*



CARCINOGENICITY

bis(Chloroethyl) nitrosourea (BCNU) is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC V.26, 1981; IARC S.4, 1982; IARC S.7, 1987). When administered intraperitoneally or intravenously, bis(chloroethyl) nitrosourea induced lung tumors including adenocarcinomas, and neurogenic tumors in rats. When administered by intraperitoneal injection, the compound induced malignant tumors in the peritoneal cavity. Other studies of bis(chloroethyl) nitrosourea in rats and mice were determined to provide insufficient data for evaluation by an IARC Working Group.

There is limited evidence for the carcinogenicity of bis(chloroethyl) nitrosourea in humans identified (IARC S.4, 1982; IARC V.26, 1981; IARC S.7, 1987). No epidemiological study on the effect of bis(chloroethyl) nitrosourea alone in humans is available, but bis(chloroethyl) nitrosourea is associated with acute nonlymphocytic leukemia following its use with other anticancer therapies in the treatment of previously existing cancer.

PROPERTIES

bis(Chloroethyl) nitrosourea is a light yellow powder that is slightly soluble in water and 50% ethanol, soluble in ethanol, and highly soluble in lipids. This compound is sensitive to oxidation and hydrolysis, subsequently forming alkylating and carbamoylating intermediates. When heated to decomposition, it emits toxic fumes of hydrochloric acid and other chlorinated compounds as well as nitrogen oxides (NO_x).

USE

bis(Chloroethyl) nitrosourea has been used since 1971 as an antineoplastic agent in the treatment of Hodgkin's lymphoma, multiple myeloma, and primary or metastatic brain tumors. It has also been reported to have antiviral, antibacterial, and antifungal activity, but no evidence was found that it is currently used in these ways (IARC V.26, 1981).

PRODUCTION

The USITC does not list any production volume for bis(chloroethyl) nitrosourea (USITC, 1995). In addition, current sources, such as *Chemcyclopedia 98* and the 1998 *Chemical Buyers Directory*, provide no suppliers of the compound (Rodnan, 1997; Tilton, 1997). In 1981,

bis(chloroethyl) nitrosourea was believed to be produced by only one U.S. company in an undisclosed amount and was available in the United States in vials containing 100 mg (IARC V.26, 1981).

EXPOSURE

The primary routes of potential human exposure to bis(chloroethyl) nitrosourea are injection, inhalation, and dermal contact. It is administered to patients in doses of 100-250 mg/m^2 body surface by intravenous injection daily, for courses of 2 or 3 days (IARC V.26, 1981). The National Occupational Exposure Survey (1981-1983) estimated that 5,596 total workers, including 2,809 women, potentially were exposed to bis(chloroethyl) nitrosourea in the work place (NIOSH, 1984). Potential exposure of health professionals who handle this drug (e.g., pharmacists, nurses, and physicians) may occur during drug preparation, administration, or cleanup; however, the risks can be avoided through use of containment equipment and proper work practices (Zimmerman et al., 1981). Potential occupational exposure to bis(chloroethyl) nitrosourea may also occur for workers involved in the formulation and packaging of the pharmaceuticals. bis(Chloroethyl) nitrosourea is not known to be a naturally occurring compound (IARC V.26, 1981).

REGULATIONS

bis(Chloroethyl) nitrosourea is used as a pharmaceutical and in low quantities relative to other chemicals; therefore, it is of little regulatory concern to EPA. However, there may be a small pollution problem relative to hospital wastes. FDA regulates bis(chloroethyl) nitrosourea under the Food, Drug, and Cosmetic Act (FD&CA) as a prescription drug, approved for human use. FDA requires warning labels on bis(chloroethyl) nitrosourea regarding its potential carcinogenicity, mutagenicity, teratogenicity, and/or fertility impairment. OSHA regulates bis(chloroethyl) nitrosourea under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-14.